CLAIMS

What is claimed is:

1. A purified and isolated caspase polypeptide comprising an amino acid sequence that is at least about 98% identical to 30 contiguous amino acids of an amino acid sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 2, 4, 6, 8, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79.

2. A purified and isolated caspase polypeptide comprising at least about 20 contiguous amino acids of an amino acid sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 2, 4, 6, 8, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79.

3. A purified and isolated caspase polypeptide according to claim 2 comprising at least about 40 contiguous amino acids of an amino acid sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 2, 4, 6, 8, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79.

4. A purified and isolated caspase polypeptide according to claim 1 comprising an amino acid sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 2, 4, 6, 8, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79.

5. A purified and isolated caspase polypeptide according to claim 1 or 2 comprising at least one subunit of human caspase-12.

6. A purified and isolated caspase polypeptide according to claim 1 or 2 comprising an amino acid sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 39, 41, 42, 43, 48 and 49.

7. A purified and isolated caspase polypeptide according to claim 1 encoded by a polynucleotide that hybridizes under stringent conditions to a nucleotide sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 1, 3, 5, 7, 9, 10, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78 and the non-coding strands thereof.

8. A purified and isolated fusion polypeptide comprising a caspase polypeptide according to claim 1.

9. A purified and isolated polynucleotide that encodes a caspase polypeptide according to any one of claims 1 through 8.

10. A purified and isolated polynucleotide that is at least about 98% identical to 100 contiguous nucleotides of a nucleotide sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 1, 3, 5, 7, 9, 10, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78 and the non-coding strands thereof, said polynucleotide encoding a caspase polypeptide.

11. A purified and isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 1, 3, 5, 7, 9, 10, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78 and fragments thereof of at least about 18 consecutive nucleotides that specifically hybridizes to any one of SEQ ID NOS: 1, 3, 5, 7, 9, 10, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76 or 78.

12. The purified and isolated polynucleotide of claim 11 comprising at least about 500 contiguous nucleotides of a nucleotide sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 1, 3, 5, 7, 9, 10, 50,

52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76 and 78, said polynucleotide encoding a caspase polypeptide.

13. The purified and isolated polynucleotide of claim 11 comprising a nucleotide sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 1, 3, 5, 7, 9, 10, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76 and 78.

14. A purified and isolated polynucleotide that hybridizes under highly stringent conditions to a nucleotide sequence selected from the group consisting of sequences set forth in SEQ ID NOS: 1, 3, 5, 7, 9, 10, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78 and the non-coding strands thereof, said polynucleotide encoding a caspase polypeptide.

15. A vector comprising a polynucleotide according to claim 9.

16. A vector comprising a polynucleotide according to any one of claims 10 through 14.

17. A purified and isolated polynucleotide comprising the polynucleotide of claim 9 operatively linked to an expression control sequence.

18. A purified and isolated polynucleotide comprising the polynucleotide of any one of claims 10 through 14 operatively linked to an expression control sequence.

19. The polynucleotide according to claim 17, wherein the expression control sequence is a promoter sequence that promotes expression of said polynucleotide in a eukaryotic cell.

20. The polynucleotide according to claim 18, wherein the expression control sequence is a promoter sequence that promotes expression of said polynucleotide in a eukaryotic cell.

21. The polynucleotide according to claim 17, wherein the expression control sequence is a heterologous promoter that promotes expression of the polynucleotide in a human cell.

22. The polynucleotide according to claim 18, wherein the expression control sequence is a heterologous promoter that promotes expression of the polynucleotide in a human cell.

23. A host cell comprising the polynucleotide of claim 17.

24. A host cell comprising the polynucleotide of claim 18.

25. A host cell comprising the polynucleotide of claim 22.

26. A host cell modified to promote transcription or translation of a human caspase-12 polynucleotide.

27. The host cell of claim 26 wherein said host cell is transformed or transfected with a heterologous polynucleotide sequence that acts as a transcription factor.

28. A method for producing a caspase polypeptide comprising the steps of growing a host cell according to claim 23 in a nutrient medium and isolating said polypeptide from said cell or said medium.

29. A method for producing a caspase polypeptide comprising the steps of growing a host cell according to claim 24 in a nutrient medium and isolating said polypeptide from said cell or said medium.

30. A method for producing a caspase polypeptide comprising the steps of growing a host cell according to claim 25 in a nutrient medium and isolating said polypeptide from said cell or said medium.

31. An antibody specific for the polypeptide of claim 4.

32. The antibody of claim 31, wherein said antibody is a monoclonal antibody.

33. A hybridoma that produces an antibody according to claim 32.

34. A method for identifying a candidate inhibitor of human caspase-12 comprising the steps of:

contacting a composition comprising a caspase polypeptide according to claim 1 or 5 with a substrate, and

measuring enzymatic activity of said caspase polypeptide in the presence and absence of a test compound,

wherein a decrease in enzymatic activity means that the test compound is a candidate inhibitor.

35. A method for identifying a candidate activator of human caspase-12 comprising the steps of:

contacting a composition comprising a caspase polypeptide according to claim 1 or 5 with a substrate, and

measuring enzymatic activity of said caspase polypeptide in the presence and absence of a test compound,

wherein an increase in enzymatic activity means that the test compound is a candidate activator.

36. A method for identifying a candidate activator of human caspase-12 comprising the steps of:

contacting a composition comprising a caspase polypeptide lacking an active site sequence, a caspase polypeptide having an active site sequence and a substrate, and

measuring enzymatic activity of said composition in the presence and absence of a test compound,

wherein a change in enzymatic activity means that the test compound is a candidate modulator.

37. A method for identifying a compound that binds to human caspase-12 comprising the steps of:

contacting a composition comprising a caspase polypeptide according to claim 1 or 5 with a test compound, and

measuring binding of said test compound to said caspase polypeptide.

38. A method for identifying a candidate inhibitor of binding of human caspase-12 to a binding partner comprising the steps of:

contacting a caspase polypeptide according to claim 1 or 5 with said binding partner in the presence and absence of a test compound, and

detecting binding of said caspase polypeptide to said binding partner,

wherein a decrease in binding in the presence of a test compound means that said test compound is a candidate inhibitor.

39. The method of claim 38 wherein said binding partner is a peptide substrate capable of proteolytic cleavage by human caspase-12.

40. A method of using a compound according to claim 38 in the manufacture of a medicament for preventing or treating a disorder involving inappropriate apoptosis or excessive cell proliferation.

41. A method for treating a disorder involving inappropriate apoptosis comprising the step of administering to a subject in need thereof a therapeutically effective amount of a novel inhibitor of human caspase-12.

42. The method of claim 41 wherein said inhibitor of human caspase-12 is identified using a screening method according to any one of claims 31, 33, 34 or 35.

43. The method of claim 41 wherein said disorder involving inappropriate apoptosis is an inflammatory disease.

44. The method of claim 41 wherein said disorder is a neurodegenerative disease.

45. A method for treating a disorder involving excessive cell proliferation comprising the step of administering to a subject in need thereof a therapeutically effective amount of a human caspase-12.

46. The method of claim 45 wherein said disorder is a cancer.

47. The method of claim 41 wherein said disorder is a cardiovascular disease.

48. The method of claim 41 wherein said disorder is characterized by a gradual and prolonged development of apoptosis.

49. A method of delivering a human caspase-12 polynucleotide to a subject comprising administering a vector comprising said human caspase-12 polynucleotide to said subject.